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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

ROBINSON, BINTA M

ART UNIT

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/539,531	Applicant(s) FRALEY ET AL.	
	Examiner BINTA M. ROBINSON	Art Unit 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2, 6, 7, 8, 9, 10, 11, 13 -15, 17, 19 is/are pending in the application.
4a) Of the above claim(s) 10, 17 and 19 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 7 is/are allowed.
- 6) ☒ Claim(s) 2, 6, 9 and 13-15 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____. |

1. Detailed Action

2. Claims 10, 17, 19 are withdrawn from consideration as being drawn to a non-elected invention.

3. The 102 (b) rejection over Hcaplus 112:97889 and over Hcaplus 1999:287417 are rendered moot in light of applicant's remarks and amendments.

4. (modified rejections)

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2, 9, 10, 13, 14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using the compounds of formula I with R1 equal to substituted carbonyl moiety as claimed, R6 equal to phenyl optionally substituted as claimed, R9 equal to hydrogen or -(CH₂)₃NH₂, R8 equal to phenyl optionally substituted as claimed, does not reasonably provide enablement for using the compounds of formula I with, R1, R6, R8, R9 equal to all other moieties claimed. The specification does not enable any skilled pharmacologist or physician to use the invention commensurate in scope with these claims. The factors to be considered in making an enablement rejection have been summarized above.

a) Determining if any particular claimed compounds with radicals R1, R6, R8 and R9 would be active would require synthesis of the substrate and subjecting it to testing with Applicants' immunofluorescence microscopic assays, cell proliferation assays, mitotic arrest and apoptosis by FACS assay, protein purification assay, and Kinesin ATPase In vitro assay. Considering the large number of compounds to be made this is a large quantity of experimentation. b) The direction concerning the claimed compounds is found at page 46, lines 20-25 which merely states Applicants' intent to make and use such compounds. c) In the instant case, none of the working examples contains any radicals R1, R6, R8 and R9 equal to the moieties claimed other than those stated to be enabled above. d) The nature of the invention is inhibition of mitotic kinesins and treatment of human diseases with Applicants' compounds. This involves physiological activity. The nature of the invention requires an understanding of the mitotic kinesins, the binding activity of small ligands to that mitotic kinesins, and the ability of those compounds to inhibit mitotic kinesins. In view of the unpredictability of receptor binding activity and claimed divergent substituents with varied polarity, size, and polarisability, the skilled physician would indeed question the inclusion of such diverse

rings, commensurate in scope with these claims. Also see the MPEP § 2164.03 for enablement requirements in the structure sensitive arts of pharmacology and medicinal chemistry.

e) There is no reasonable basis for the assumption that the myriad of compounds embraced the present formula (I) will all share the same biological properties. The diverse claimed compounds are chemically non-equivalent and there is no basis in the prior art for assuming in the non-predictable art of pharmacology that structurally dissimilar compounds will have such activity, *In re Surrey* 151 USPQ 724 (compounds actually tested which demonstrated the asserted psychomotor stimulatory and anti-convulsant properties were those having the 3,4-dichlorophenyl substituent at the 2-position on the thiazolidone nucleus not sufficient for enablement of any heterocyclic radical at the same position). *In re Fouche*, 169 USPQ 429 at 434 (a Markush group including both aliphatic and heterocyclic members not enabled for the use of those compounds within the claim having heterocyclic moieties.) *In re CAVALLITO AND GRAY*, 127 USPQ 202 (claims covering several hundred thousand possible compounds, of which only thirty are specifically identified in appellants' application, not enabled unless all of the thirty specific compounds disclosed had equal

hypotensive potency because that fact would strongly indicate that the potency was derived solely from the basic structural formula common to all of them. A wide variation in such potency would suggest that it was due in part to the added substituents and might be eliminated or even reversed by many of the possible substituents which had not been tried.)

f) The artisan using Applicants' invention to treat diseases with the claimed compounds would be a physician with a MD degree and several years of experience. He would be unaware of how to predict *a priori* how a changing a heterocyclic ring would affect biological activity. In view of the divergent rings with varied basicity, steric hindrance, and polarisability, the skilled physician would indeed question the inclusion of such fused rings, commensurate in scope with these claims. g) Physiological activity, is well-known to be unpredictable, *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *In re Vaeck*, 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). h) The breadth of the claims includes all of millions of compounds of formula (I). Thus, the scope is very broad. The present claims embrace various

heterocyclic radicals, which are not art-recognized as equivalent. The specific compounds made are not adequately representative of the compounds embraced by the extensive Markush groups instantly claimed.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

6. Paragraph 8.28

Claims 2, 9, 11, 13, 14, 15 are directed to an invention not patentably distinct from claims 1-5, 10, 12, 13, 14-16 of commonly assigned 10539512, US PG Pub 20060052611. Specifically, Copending Application No. 10539512, US PG Pub 20060052611 teaches the instant compound, composition, and process of making them. The difference between the prior art compound and the instantly claimed compounds is the teaching of a genus of compounds, compositions, and a process of making these products which overlap in subject matter with the instant compounds, compositions, and a process of making the instant products. It would have been obvious to one of ordinary

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skill in the art to select various known radicals within a genus to prepare structurally similar compounds. For instance, see the compound, 1-acetyl-4-(2,5-difluorophenyl)-6-phenyl-1,2,3, 6-tetrahydropyridine, where a disclosed species is exemplified.

Accordingly, the compounds, compositions, and process of preparing them are deemed unpatentable therefrom in the absence of a showing of unexpected results for the claimed compounds, compositions and a process of preparing them over those of the generic prior art compounds, compositions and a process of preparing these products.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned US PG Pub 20060052611, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as

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to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 2, 9, 11, 13, 14, 15 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5, 10, 12, 13, 14-16 of copending Application No. 10539512, US PG Pub 20060052611. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant application claims a genus of compounds of formula I, compositions, and a process of making these products which overlap in subject matter with the copending application's genus of compounds of formula I, compositions, and a process of making these products.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

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Copending Application No. 10539512, US PG Pub 20060052611 teaches the instant compound, composition, and process of making them. The difference between the prior art compound and the instantly claimed compounds is the teaching of a genus of compounds, compositions, and a process of making these products which overlap in subject matter with the instant compounds, compositions, and a process of making the instant products. It would have been obvious to one of ordinary skill in the art to select various known radicals within a genus to prepare structurally similar compounds. For instance, see the compound, 1-acetyl-4-(2,5-difluorophenyl)-6-phenyl-1,2,3, 6-tetrahydropyridine, where a disclosed species is exemplified. Accordingly, the compounds, compositions, and process of preparing them are deemed unpatentable therefrom in the absence of a showing of unexpected results for the claimed compounds, compositions and a process of preparing them over those of the generic prior art compounds, compositions and a process of preparing these products.

9. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

10. Claims 6 is provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 6 of copending Application No. 10539512. This is a provisional double patenting rejection since the conflicting claims have not in fact been

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patented. Both claims claim the instant compound, 1-acetyl-4-(2,5-difluorophenyl)-6-phenyl-1,2,3, 6-tetrahydropyridine.

11. Claim 7 is allowable.

Response to Applicant's Remarks

The applicant traverses the 112, first paragraph enablement rejection and has argued that their amendments obviate the rejection. However, the claims have not been limited to those compounds which are enabled and the working examples of compounds tested in the various assays do not encompass the sufficiently representative scope of compounds being claimed or disclosed in the specification.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Binta M. Robinson whose telephone number is (571) 272-0692. The examiner can normally be reached on M-F (9:30-6:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Janet Andres can be reached on 571-272-0670.

A facsimile center has been established. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier numbers for accessing the facsimile machine are (703)308-4242, (703)305-3592, and (703)305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-1600.

/Binta M Robinson/
Examiner, Art Unit 1625

/Janet L. Andres/
Supervisory Patent Examiner, Art Unit 1625